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Left ventricular hypertrophy
Relation of structure to diastolic function in hypertension

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SUMMARY Digitised M mode echocardiography was used to determine the relation between the degree of left ventricular hypertrophy and abnormalities of isovolumic relaxation and diastolic function. Fifty six patients with varying severity of non-malignant systemic hypertension without evidence of ischaemic heart disease, left ventricular dilatation, or clinical heart failure were studied. In addition, 10 athletes with hypertrophy and 20 normal subjects were studied. Athletes and patients with moderate (systolic blood pressure 175 to 200 mm Hg) and severe hypertension (>200 mm Hg) had a significant increase in left ventricular mass. Cavity dimensions were normal in hypertensive patients and increased in athletes. Systolic function was normal in all groups. Regardless of the degree of hypertrophy patients with hypertension had a prolonged isovolumic relaxation period and delayed mitral valve opening. Patients with hypertrophy also had a reduced rate and prolonged duration of rapid early diastolic dimension increase and posterior wall thinning. Athletes, however, who had an equivalent degree of hypertrophy to patients with moderate or severe hypertension had entirely normal function. Measurements of diastolic function were significantly correlated with wall thickness and left ventricular mass. These indices of hypertrophy, particularly posterior wall thickness and the sum of posterior wall and septal thickness, were positively correlated with the duration of isovolumic relaxation and delay in mitral opening and negatively with the peak rate of early diastolic dimension increase and wall thinning.

Thus in hypertensive patients with non-dilated left ventricular hypertrophy there appears to be a relation between the degree of wall thickening and abnormalities of diastolic function.

Left ventricular hypertrophy which develops in response to pressure overload is presumably a homeostatic and beneficial process for normalising peak systolic wall stress and reducing oxygen requirement.[1] Gross systolic function (ejection fraction, peak velocity of circumferential fibre shortening, and rate of pressure rise) is often normal, but a recent study in hypertensive patients has shown that systolic left ventricular performance declines with increasing left ventricular hypertrophy.[2] Nevertheless, systolic function may be normal even in the presence of severe hypertrophy, but abnormalities of diastolic behaviour may frequently be detected. These include a raised left ventricular end diastolic pressure, prolonged and incoordinate relaxation period, reduced peak rate, and prolonged duration of left ventricular filling and wall thinning.[3–7] The purpose of this study was to determine the relation between abnormalities of diastolic function and the degree of myocardial hypertrophy in hypertensive patients.

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Patients and methods

STUDY POPULATION

Fifty six patients with non-malignant systemic hypertension without severely impaired renal function in whom high quality echocardiograms could be obtained were selected to provide a study population of patients with a widely varying degree of left ventricular hypertrophy. Left ventricular hypertrophy was diagnosed when the sum of the echocardiographic posterior wall and septal thickness exceeded two standard deviations (SD) from normal (for example >2·4 cm). All patients were in sinus rhythm without chest pain or clinical heart failure. Patients were

excluded if they had electrocardiographic evidence of myocardial infarction or bundle branch block, radiological pulmonary venous congestion, or echocardiographic left ventricular dilatation (>2SD from normal). In addition, 30 control patients (20 normal subjects and 10 athletes) were studied.

Hypertensive patients

Fifty seven patients with a wide range of blood pressures and hypertrophy were studied before or within 24 hours of starting treatment. They were divided into three groups by the degree of rise of blood pressure.

Mild hypertension (Fig. 1)—Eighteen patients, aged 22 to 58 (mean 43±8) years, 13 of whom were women, had systolic blood pressures <175 mm Hg.

Moderate hypertension—Seventeen patients, aged 19 to 55 (mean 46±11) years, had presenting systolic blood pressures ranging from 176 to 200 mm Hg; 11 were women.

Severe hypertension (Fig. 2)—Twenty one patients (11 men), aged 22 to 57 years, had systolic blood pressures >201 mm Hg.

Control subjects

Normal subjects—Twenty (10 men) healthy hospital employees aged 17 to 60 (mean 44±9) years were studied.

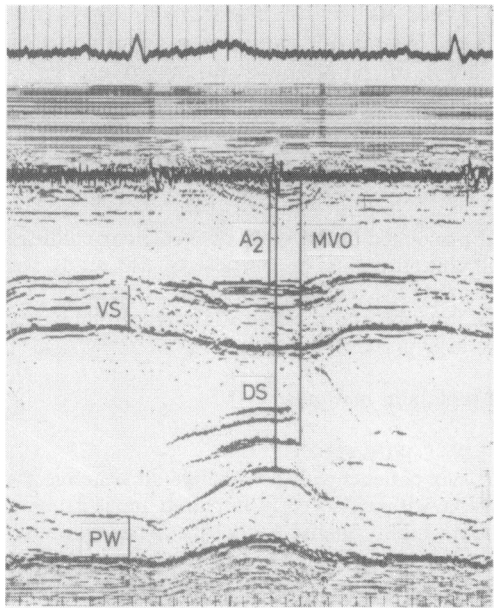

Fig. 1 *M mode echocardiogram of a patient with mild hypertension (blood pressure 165/105 mm Hg) without evidence of hypertrophy of the posterior wall (PW) or septum (VS) showing delay in the timing of mitral valve opening (MVO) from minimum cavity dimension (DS) and prolonged isovolumic relaxation.*

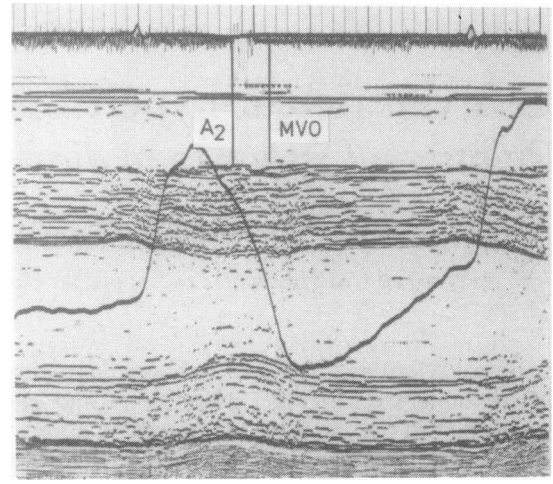

Fig. 2 *Echocardiogram of a patient with severe hypertension showing gross hypertrophy, prolonged isovolumic relaxation, and a reduced rate of wall thinning and cavity dimension increase without cavity dilatation. MVO, mitral valve opening.*

Athletes—Ten top class endurance swimmers (more than one hour daily exercise), all men aged 16 to 32 (mean 24±3) years with echocardiographic evidence of left ventricular hypertrophy were studied (Fig. 3).

ESTIMATION OF LEFT VENTRICULAR STRUCTURE AND FUNCTION

The patients were examined in the partial left lateral position with a SK20 Ultrasonoscope and a Cambridge multichannel photographic recorder or an Electronics for Medicine Echo IV. Echocardiograms were recorded with simultaneous apexcardiograms, phonocardiograms, and electrocardiograms at a paper speed of 100 mm/s. A left ventricular echocardiogram at the level of the tips of the mitral valve (to define onset of cusp opening) showing clear continuous echoes from both the septum and posterior wall was used for further analysis. The thickness of the septum and posterior wall were measured (cm) at end diastole (Q wave, electrocardiogram).

Echocardiograms were digitised as previously described by Gibson and Brown[8] using a Summagraphics digitiser and a Prime 750 computer system. From the records the following measurements were made: *(a)* end diastolic (Q wave, electrocardiogram) and end systolic cavity dimension (at minimum cavity size) (cm); *(b)* peak rates of increase in dimension and posterior wall thinning during early diastole (cm/s); *(c)* early diastolic filling period, defined as the period from minimal left ventricular dimension to the time of

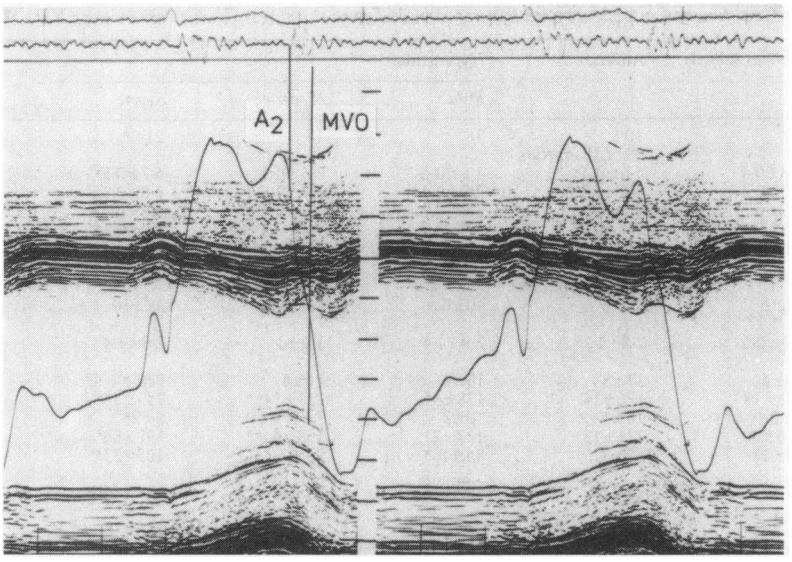

Fig. 3 *M mode echocardiogram with simultaneous phonocardiogram, apexcardiogram, and electrocardiogram from a top class long distance swimmer showing normal function and symmetrical hypertrophy. Note normal interval from A_2 to mitral valve opening (MVO).*

reduction in the rate of dimension increase to 20% of its peak value (ms); *(d)* interval from maximum posterior wall thickness to its decline to 20% of the peak rate of thinning, arbitrarily defined as the duration of rapid wall thinning (ms); and *(e)* time intervals (ms)—phonocardiographic A_2 to the onset of mitral valve opening (isovolumic relaxation) and minimum cavity dimension to mitral valve opening.

(a) Fractional shortening was calculated as (DD−DS)/DD×100. *(b)* Left ventricular mass was used to determine relation of structure and function and as all equations give proportionate results, the simplest—for example, cube formula—was used. Mass was calculated as 1·055 [(VS+PW +DD)3−DD3] where VS and PW are septal and posterior wall thickness and DD and DS are the diastolic and systolic left ventricular cavity dimensions. *(c)* Change in dimension during isovolumic relaxation was expressed as a percentage of the total dimension change during the cardiac cycle. Incoordinate relaxation was diagnosed when this value exceeded ±2SD from normal—for example 15%.

STATISTICAL METHOD

Values are expressed as mean±one standard deviation. Student's *t* test (unpaired) was used to test differences between normally distributed variables and Mann-Whitney U test between variables with a skewed distribution. The relation between continuous distributed variables was determined by the use of Pearson's correlation coefficient (r).

Results

LEFT VENTRICULAR STRUCTURE AND FUNCTION

Measurements of left ventricular posterior wall and septal thickness, dimension, and mass are summarised in Table 1. Left ventricular cavity dimensions were within the normal range in hypertensives, but the diastolic dimension was increased in athletes ($p<0·001$). Athletes and moderate and severe hypertensives had significant thickening of the posterior wall and septum and increased mass ($p<0·001$).

There were abnormalities of left ventricular function in all groups of hypertensives, but athletes who had equivalent degrees of hypertrophy to moderate or severe hypertensives had entirely normal function. In all subject groups fractional shortening and peak velocity of circumferential fibre shortening were normal (Table 1). In hypertensives, isovolumic relaxation was prolonged ($p<0·001$), mitral valve opening was delayed from minimum dimension ($p<0·001$), and significant cavity dimension increase ($p<0·001$) was seen during isovumic relaxation ($p<0·01$). These abnormalities were also observed in mild hypertensives without echocardiographic evidence of hypertrophy.

In normals, A_2 preceded minimum dimension by 53±17 ms. In all hypertensive groups, A_2 preceded minimum dimension. There was, however, a wide range of values, and this interval was significantly reduced from normal ($p<0·01$) in the moderate (18±29 ms) and severe (6±19 ms) hypertensive

Table 1 *Left ventricular (LV) structure and function in patients with hypertension and control subjects. Values are means±SD*

	Normal subjects	*Athletes*	*Hypertension*		
			Mild	*Moderate*	*Severe*
No of subjects	20	10	18	17	21
		LV structure			
Diastolic dimension (cm)	4·8±0·4	5·6±0·4*	4·6±0·6	4·5±0·5	4·7±0·5
Systolic dimension (cm)	3·0±0·4	4·0±0·3**	2·8±0·4	2·7±0·5	3·0±0·7
Posterior wall (cm)	0·9±0·1	1·2±0·1*	1·0±0·2	1·3±0·1*	1·8±0·4*
Septum (cm)	0·9±0·1	1·4±0·1*	1·0±0·2	1·4±0·2*	1·9±0·4*
LV mass (cm)	185±50	386±58*	203±44	289±47*	528±205*
		LV function			
Fractional shortening (%)	39±6	34±6	40±6	41±7	38±10
Peak velocity of circumferential fibre shortening (per s)	2·4±0·5	2·8±1	2·9±1·4	3·0±1	2·9±1·4
Peak rate of dimension increase (cm/s)	15±4	17±3	16±4	11±4	9±3*
Duration of filling (ms)	181±18	176±14	178±35	211±54**	249±58*
Peak rate of thinning (cm/s)	9±2	10±1	10±3	7±2**	5±2*
Duration of thinning (ms)	116±30	121±13	122±21	158±44**	197±60*
Isovolumic relaxation period (ms)	63±11	57±8	84±16*	96±22*	105±23*
Minimum dimension to mitral valve opening (ms)	10±7	16±16	43±24*	78±34*	99±25*
Dimension change before mitral valve opening (%)	5±5	1·5±4	13±9**	21±8*	31±11*

Difference from normal: *p<0·001, **p<0·01.

groups. In some patients in the latter two groups minimum dimension could precede A_2.

In early diastole the peak rate of dimension increase was reduced in severe hypertensives, and the early diastolic filling period was prolonged (p<0·001). There was a reduction in the peak rate (p<0·01) and increase in duration (p<0·01) of the initial rapid phase of wall thinning in moderate and severe hypertensives.

RELATION OF STRUCTURE AND FUNCTION

Measurements of diastolic function were significantly correlated with indices of hypertrophy especially posterior wall thickness and the sum of posterior wall and septal thickness (Table 2). These indices of hypertrophy showed a significant positive correlation (p<0·001) with delay in mitral valve opening (r=0·57 to 0·7), prolonged isovolumic relaxation (r=0·44 to 0·52), and dimension change during isovolumic relaxation (r=0·56 to 0·67). The peak rate of dimension increase was negatively (r=0·42 to 0·55), and its duration positively (r=0·47 to 0·59), related to the degree of hypertrophy. A similar relation was seen with the peak rate (r=0·41 to 0·55) and duration of posterior wall thinning (r=0·34 to 0·51). Systolic measurements of function were not significantly correlated with the degree of hypertrophy.

Discussion

In this study we examined the relation between the altered diastolic behaviour of the left ventricle and the degree of hypertrophy expressed as wall thickness and mass. Digitised M mode echocardiography was used as it allows localisation of epicardium as well as endocardium at an adequate rate throughout the cardiac cycle, features which are necessary for the study of left ventricular diastolic behaviour.[8 9] Normally A_2 precedes minimum dimension by 36-60 ms, and mitral valve opening defines the end of isovolumic

Table 2 *Relation of left ventricular (LV) hypertrophy to function in 56 patients with hypertension. Pearson's correlation coefficient (r)*

	Posterior wall	*Posterior wall plus septum*	*LV mass*
Fractional shortening	0·1	0·1	0·02
Peak velocity of circumferential fibre shortening	0·29	0·31	0·28
Peak rate of dimension increase	−0·5*	−0·55*	−0·42**
Duration of filling	0·56*	0·59*	0·47*
Peak rate of wall thinning	−0·51*	−0·57*	−0·41**
Duration of thinning	0·44*	0·5*	0·34**
Isovolumic relaxation period	0·51*	0·52*	0·44*
Minimum dimension to mitral valve opening	0·62*	0·7*	0·57*
Dimension change before mitral valve opening	0·67*	0·66*	0·56*

Significances: *p<0·001, **p<0·01.

relaxation; thereafter changes in wall thickness occur synchronously with those of filling so that maximum wall thickness coincides with minimum cavity dimension and the onset of mitral valve opening.[10]

In patients with hypertension isovolumic relaxation was prolonged, and mitral valve opening delayed, and was usually acccompanied by an increase in cavity dimension during isovolumic relaxation even in the absence of hypertrophy. Prolonged left ventricular ejection time and delayed A_2 are well recognised features in aortic stenosis,[11] but A_2 and minimum dimension may be almost synchronous in some patients with hypertension.[12 13] In addition, this may occur in ischaemic heart disease,[12] where it correlates with evidence of incoordinate systolic wall motion. In left ventricular hypertrophy, abnormalities of wall motion in late systole presumably disturb the relative timing of A_2 and minimum dimension. Prolonged and incoordinate relaxation has been previously reported in left ventricular hypertrophy.[4] We have shown that these abnormalities were significantly correlated with the degree of hypertrophy and were absent in only nine patients with hypertension. If patients with raised left ventricular end diastolic pressure (which has the effect of reducing the duration of relaxation)[14] had been included this relation probably would not have been found. Such abnormalities may also be found in hypertrophic cardiomyopathy,[4] and although prolonged and incoordinate relaxation may be properties of the hypertrophied myocardium these are not specific abnormalities and may be found in isolated ischaemic papillary muscles[15] and diabetic patients without hypertrophy.[16] In addition, reduction of hypertrophy by treating hypertension and aortic coarctation does not correct impaired relaxation.[7 17]

After mitral valve opening a period of rapid left ventricular filling occurs lasting 120–200 ms. Previous studies using echocardiography and angiocardiography have shown that this may be abnormal in left ventricular hypertrophy.[4 5 18] We confirmed that the peak rate of dimension increase may be reduced and its duration prolonged in patients with hypertrophy, and there was a significant correlation between measurements during filling and the degree of myocardial hypertrophy. The mechanism of early rapid diastolic filling is ill understood: it is not due simply to left atrial/ventricular pressure difference[19] but may be due to the recoil of elastic forces. This may be shown as echocardiographic rapid wall thinning, which normally has a peak rate of 8–12 cm/s and lasts for 90–140 ms. In hypertrophy, the peak rate of posterior wall thinning may be reduced and prolonged in duration, and this is also significantly related to the degree of hypertrophy. This would suggest that impaired wall thinning is due to altered behaviour of the hypertrophied myocardium in a smaller fashion to relaxation.[10]

The correlations found between indices of hypertrophy and abnormal diastolic properties do not prove a causal relation, especially as the component of myocardial structure by which they are determined is unknown. Myocardial hypertrophy is presumably a homeostatic mechanism, and why athletes do not develop abnormalities of function, whereas equivalent degrees of hypertrophy in secondary hypertrophy result in pronounced impairment, is also unknown. In general, however, hypertensive patients without posterior wall thickening had isovolumic relaxation abnormalities alone, and those with hypertrophy also had impaired wall thinning and filling. Other factors may also be important in altering diastolic function in hypertrophy especially myocardial ischaemia and fibrosis, and the latter has been shown to increase with greater severity of hypertrophy.[20] Previous studies have found that patients with hypertrophy of various causes had similar abnormalities of diastolic function, and our results suggest that these are significantly related to the degree of hypertrophy. We found that while fractional shortening and therefore derived indices of pump function and cardiac output remain relatively normal in hypertensive left ventricular hypertrophy diastolic function is frequently impaired. This included prolonged and incoordinate relaxation and reduced peak rate of cavity dimension increase and posterior wall thinning. In contrast, athletes, who had an equivalent degree of hypertrophy, had entirely normal function.

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